66. (Allowed) An isolated peptide consisting of the sequence of any one of SEQ ID NO:3 through SEQ ID NO:76.

For the convenience of the Examiner, a marked-up copy of the pending claims as amended is attached hereto as "Exhibit A." A Clean copy of all pending claims following entry of the present amendment is attached hereto as "Exhibit B."

Applicant notes for the record that all pending claims were free from rejection under the utility (35 U. S. C. §101) and prior art (35 U. S. C. §102 and 35 U. S. C. §103) sections of the Statutes.

Applicant appreciates the fact that the present Examiner has recognized the allowability of claims 12 and 66, and further recognizes the progress made by Applicant in the previous response in addressing certain of the previous Examiner's concerns with respect to claim clarity.

Applicant also appreciates the concurrence of the present Examiner that the pending claims are free of any prior art concerns, and that the final remaining issues to be resolved before allowance of the case primarily concern issues of claim definiteness and language clarity in the claims.

2.2 THE REJECTION OF CLAIMS 1-9, 32-37, 44-45, 47, 49-52, 64-65, AND 67-75 UNDER 35 U. S. C. § 112, 2ND PARAGRAPH, HAS BEEN OVERCOME.

(Re: the Action, Items 4-5)

Claims 1-9, 32-37, 44-45, 47, 49-52, 64-65, and 67-75 were rejected under 35 U.S.C. 112, 2nd paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant respectfully traverses, but appreciates the comments of the current Examiner with respect to improving the clarity of the lower end of the range of peptide lengths. In that

regard, Applicant has amended the peptide claims in recognition of the fact that the shortest peptide sequence recited in the pending claims (SEQ ID NO:4) is 14 amino acids in length. Thus, the clarity issue with respect to the lower limit of peptide length is now resolved.

Likewise, a review of the Examiner's comments with respect to certain enablement and written description issues also cited in the Action revealed that claims 1 to 9 lacked sufficient clarity with respect to the upper length of the recited range, particularly in view of the fact that the length of the various peptides disclosed in SEQ ID NO:3-76 were of varying lengths. As such, the lack of clarity of language in these claims made an interpretation of the enablement and written description questions difficult. As such, Applicant has improved the language of claims 1 to 9 to properly take into account the physical lengths of the various peptides disclosed in SEQ ID NOs:3-76. As such, the Applicant now believes that not only has he fully addressed the current and previous Examiner's concerns with respect to clarity of the claim language (and specifically the rejections under §112, 2nd, but also this improved clarity has removed the issue of concern expressed by the Examiner with respect to the remaining §112, 1st, issues. Now, Applicant believes that these clarifications overcome the rejection of these claims under both parts of 35 U.S.C. §112. Applicant respectfully requests that the rejection be withdrawn and that the claims proceed to allowance.

Various claims remain rejected from the previous Action for use of the terms "about" and "at least a first" allegedly because the words are ambiguous and make the claims indefinite.

Applicant respectfully traverses, and again reminds the Office that the thrust of this rejection is at odds with long-established examination practice and case law and is therefore unsustainable.

Applicant's representative has again reviewed in detail M. P. E. P. § 2173, and the relevant case law concerning the criteria for assessing compliance with 35 U. S. C. § 112, 2nd paragraph, and can find nothing to indicate that the present claims are indefinite by the use of terms including the phrases "about" and "at least" (such as at least a first, at least a second, *etc.*). In fact, these sections of the M.P.E.P. provide that Applicant(s) can "define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art" (M. P. E. P. §2173.01, at page 2100-145, column 2). As the terms "at least a first", "at least a second" and such like in the claims are not used in a manner contrary to their ordinary meanings, and the claimed range clearly defines an upper and a lower limit, the claims are sufficiently definite and the rejection should be withdrawn.

In a response to the previous Action, Applicant pointed out that such language is widespread in issued U. S. patents in the same general field as that of Applicant's. See for example, U.S. Patents 5.853,987 (see *e.g.,* claims 1-7 and 62), 3,933,430 (see *e.g.,* claim 1), and 4,981,782 (see *e.g.,* claim 1). The present Action, however, is silent on Applicant's previous argument, and instead the present Action merely repeats the language of the previous Action and argues that "one skilled in the art could not determine how long the amino acid sequence should be, or it if should be the exact number of residues as recited." The Applicant again urges the Examiner to consider the claims of these patents as evidence that the use of these terms is proper and acceptable under current USPTO TC1600 practice.

M. P. E. P. § 2173.05(b)A is also very clear that the term "about" may be used define an end of a range of numbers with flexibility *and* with definite clarity. The phrase "a peptide of from 14 to about 40 amino acids in length" is readily understood to mean that the length of the claimed peptide (at its lower range) is no shorter than 14 amino acids in length, and that (on its

upper range) it may be about or approximately 40 amino acids in length (*i.e.*, it may be 38 amino acids in length, 39 amino acids in length, 40 amino acids in length, 41 amino acids in length, *etc.*). The term simply means "approximately." One reading a claim that recites "a peptide of from 14 to about 30 amino acids in length" would understand that the peptide would be at least 14 amino acids in length, and not longer than approximately 30 amino acids in length (*i.e.*, approximately 29 or 30 or 31 amino acids in length). The term means "approximately," and its use is clear and concise.

The term "at least about" also is not *prima facie* indefinite. This point was specifically addressed in the *Amgen v. Chugai Pharmaceutical Co.* decision cited in M. P. E. P. §2173.05(b)A. The Court in its decision cautioned against over-interpretation of the specific decision in that particular case as a basis to apply a specific finding of indefiniteness in that case, to a prohibition of the use of the terms "about" and "at least about" in all patent cases.

The Amgen court stated:

> "In arriving at this conclusion, we caution that our holding that the term "about" renders indefinite claims 4 and 6 should not be understood as ruling out any and all uses of this term in patent claims. It may be acceptable in appropriate fact situations, *e.g., W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1557, 220 U.S.P.Q. (BNA) 303, 316 (Fed. Cir. 1983)* ("use of 'stretching . . . at a rate exceeding about 10% per second' in the claims is not indefinite"), even though it is not here."

Moreover, in the Amgen decision, the specific facts of that case concerned Applicant's amendment of particular claims to include the phrase "at least about" in order to overcome close prior cited during prosecution. The Amgen Court also specifically noted this fact in their Opinion stating that:

> "When the meaning of claims is in doubt, especially when, as is the case here, there is close prior art, they are properly declared invalid. *Standard Oil Co. v. American Cyanamid Co., 774 F.2d 448, 453, 227 U.S.P.Q. (BNA) 293, 297 (Fed. Cir. 1985). (emphasis added).*"

In the present case, however, there is no prior art cited against the claims, and there has been no amendment by Applicant to include the "at least about" language in an attempt to distance itself from any cited prior art. The language has been used throughout the prosecution of the pending claims, and the use of both terms "about" and "at least about" are plain and definite in the context of the present application. As such, the indefiniteness rejection is improper. Applicant respectfully requests the Office's concurrence with same and removal of this rejection. None of the claims recited an open-ended range without an upper limit, which was important in the specific facts of the Amgen ruling.

However, without acquiescing in any way, and solely in an effort to demonstrate even more clarity in the present case, and to work with the Office to achieve an expedient and cost-effective allowance of the claimed subject matter, Applicant has noted that the previous Examiner-in-Charge of the case has recommended the use of the term "approximately" as a substitute for the word "about." Since Applicant considers the terms "about" and "approximately" to be equivalent, claims 67 to 75 have been amended to replace the term "about" with "approximately," as previously suggested by Examiner Jamroz to be definite and free from rejection.

Likewise, without acquiescing in any way, and solely in an effort to proceed claims to particular embodiments of the invention to timely allowance and issue, Applicant notes that the use of the phrase "at least one component" in Claim 51 has not been specifically objected to by either Examiner Jamroz or Examiner Belyavskyi as being indefinite, and since Applicant considers the phrases "at least a first component" and "at least one component" to be both equivalent and interchangeable, Applicant has amended the language of claims 32, 37, 43-45, 47, and 49 to replace the phrase "at least a first" with "at least one" in an effort to provide more clarity. While Applicant maintains his original position that the terms "at least a first" is clearly

understood to mean "one or more" or "at least one," and while both phrases used in the claims are definite and well-understood, Applicant provides the amendment to offer even more improved clarity of claim language and thus allowance of the claims.

In conclusion, Applicant now believes that all claims are free from further rejection under this section of the Statute, and respectfully requests that the rejection be withdrawn.

2.3 THE REJECTION OF CLAIMS 33-37 UNDER 35 U. S. C. §112, 1ST PARAGRAPH, HAS BEEN OVERCOME.

(Re: the Action, Items 6 and 7)

Claims 33 to 37 remain rejected under 35 U. S. C. §112, 2nd paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor was in possession of the claimed invention when the application was filed. The Action on page 3, Item 7 states that this rejection is a "New Matter" rejection.

Applicant again respectfully traverses, and points out once again that this rejection ***cannot be properly considered a "new matter" rejection, since the literal claim language now in question was present in originally-filed claims 32-37*** (see original Specification and claims).

The Action at page 4 states "The specification and the claims as originally field (*sic*) only support (*sic*) antibody or antigen-binding fragment (*sic*) that comprising (*sic*) a first detectable label, wherein radiolabel (*sic*) comprises 3H, 14C, 32P, 35S, 90Y, 99Tc, 125I, or 131I (*sic*)....."

Applicant respectfully traverses and rejects this misinterpretation of the plain language of the original claim which read:

> 32. The peptide of claim 1, the polypeptide of claim 11, or the antibody or antigen-binding fragment of claim 13, further comprising at least a first detectable label.

The plain and simple interpretation of this claim is that it refers to three compounds in the alternative, each of which can further comprise "at least a first detectable label." That is to say, the claim clearly encompasses three elements:

A) The peptide of claim 1, further comprising at least a first detectable label;

B) The polypeptide of claim 11, further comprising at least a first detectable label; and

C) The antibody or antigen-binding fragment of claim 13, further comprising at least a first detectable label.

To suggest that the phrase "further comprising at least a first detectable label" only applies to element "C" of the claim, and as such, the limitation does not apply to either element "A" (the peptide of claim 1), or element "B" (the polypeptide of claim 11 [now claim 12]) is unfounded and without merit.

Moreover, such a conclusion is contradictory to the clear prosecution record with regard to claim 32: On 11/23/01, a Restriction Requirement was issued by Examiner Jamroz which restricted peptides and polypeptides, as well as compositions, and kits comprising them (Group III invention) from antibody and antigen-binding fragments compositions and kits comprising them (Group IV invention).

As such, when on 1/23/02, Applicant filed a Response to Restriction and elected the Group III invention, it was proper to amend original claim 32, to remove element "C" which was drawn to antibodies and antigen-binding fragments, the now *non-elected* invention.

At the time, Applicant amended claim 32 on 1/23/02 to include only element "A":

32. (Amended) The isolated peptide of claim 1, further comprising at least a first detectable label.

The amendment was NOT a new matter rejection, and was clearly proper in view of the Office-imposed Restriction Requirement that removed element "C" from consideration in the present application.

In the subsequent first Office Action which issued on the merits, Examiner Jamroz confirmed her reconsideration of the previous restriction requirement of record and stated that:

"Claims 1-12, 32-37, and 42-52 wherein the compound, compositions thereof, and kit comprising a peptide of SEQ ID NO:3-76 and a polypeptide consisting essentially of positions 1-322 of SEQ ID NO:2 and a polypeptide consisting of positions 1-322 of SEQ ID NO:2 are under consideration in the instant application." (First Office Action, page 2).

Based upon Applicant's recognition that Examiner Jamroz was in fact considering both the peptides (element "A" of original claim 32) and the polypeptide of SEQ ID NO:2 (element "B" of original claim 32), Applicant amended claim 32 in the 7/8/02 response to the First Office Action to re-introduce element "B" into the claim. Again, the amendment was proper, since element "B" was not previously restricted away from the peptide claims (element "A"), and the polypeptide was already under consideration by the Examiner. The twice-amended claim read:

> 32. (Twice Amended) The isolated peptide of claim 1, or the polypeptide of claim 11, further comprising at least a first detectable label.

Again, it was within Applicant's purview and right to reintroduce element "B" of original claim 32, and the simple fact that Applicant chose to reintroduce element "B" into the claim, when elements "A" and "B" of claim 32 were properly under consideration in the application, **does not constitute "new matter**." The rejection is, therefore, as a matter of law, improper.

Furthermore, in the response to the present Office Action, to provide the additional clarity requested by the Examiner, and to properly depend claim 32 from claim 12 (claim 11 no longer pending), Applicant amended the claim a third time as follows:

> 32. (Thrice Amended) The isolated peptide of claim 1, or the polypeptide of claim 12, further comprising at least one detectable label.

Again, the present amendment is proper, is NOT new matter, and the original claims and specification CLEARLY enable all three elements of original claim 32, not just element "C" as the Office now contends.

To conclude that the phrase "further comprising at least a first detectable label" in original claim 32 is limited only to further define element "C" (an antibody or antigen-binding fragment), but does not further define elements "A" and "B" (the peptide of claim 1, and the polypeptide of claim 11[now claim 12], respectively) as also "further comprising at least a first detectable label" is without foundation, and in contrary to standard claim interpretation.

In summary, original claim 32 clearly defines a genus of peptide, polypeptides, antibodies, and antigen binding fragments of the invention that may further comprise at least a first detection label. Therefore, claims 33-37, drawn to particular species of that genus (*i.e.,* peptides and polypeptides), are *clearly* properly dependent, and *clearly do not encompass* "new matter." Once again, Applicant points the Examiner's attention to the language of the Specification on page 8, 2nd paragraph, which describes immunodetection methods and kits that utilize labeled antibodies, antigen binding fragments, polypeptides or peptides. That the present restriction has been imposed limiting the scope of the claims to peptides and polypeptide compositions and their uses, claims 33-37 as pending are clearly supported by the originally filed specification and original claims 32-37. Therefore, Applicant respectfully requests that this rejection be withdrawn, and that the claims be allowed to proceed to allowance.

2.4 THE REJECTION OF CLAIMS 1-8, 32-37, 42-52, 61-65, AND 67-75 UNDER 35 U. S. C. §112, 1ST PARAGRAPH, IS OVERCOME.

(Re: the Action, Item 8)

Claims 1-8, 10-11, 32-37, 42-52, 61-65, and 67-75 remain rejected under 35 U. S. C. §112, 1st paragraph, allegedly as containing subject matter which was not described in the specification in such as way as to enable one of skill in the art to make and/or use the invention.

Applicant respectfully traverses.

The present Action repeats the language of the previous Action almost verbatim, and contends that "Applicant discloses a single polypeptide comprising SEQ ID NO:2 (491 residues), a peptide consisting of residues 1-322 of SEQ ID NO:2, and peptides consisting of SEQ ID NOs:3-76 in the instant specification." (The Action, Page 5, 1st paragraph). The Action repeats the previous rejection stating that the Specification does not reasonably provide enablement for any peptide/polypeptide comprising residues 1-322 of SEQ ID NO:2, or any peptide/polypeptide from 9 to about 20/30/40/50/60/70 amino acids in length comprising at least a first contiguous sequence" according to any one of SEQ ID NO:3-76 (original emphasis).

Both the present Action, and the first Action by the previous examiner, admit, however, that "Applicant has taught how to make and use SEQ ID NOs:2-76 and residues 1-322 of SEQ ID NO:2 *to generate antibodies which bind to native p33 to serve as diagnostic markers of therapeutic efficacy of cancer treatments*." (present Action, page 8, 3rd paragraph; first Action, page 11, 3rd paragraph).

Thus, two separate Examiners have recognized that a clear, practical, substantial, credible, and real-world "use" of the claimed peptide and polypeptide compositions not only exists, but that the use was disclosed in the Specification, and, more importantly, that the ***"how to make and use"*** requirement of the Statute with respect to at least one such substantial and credible use ***has also***

been disclosed by Applicant. Furthermore, both Examiners have recognized that *the Specification has taught "how to make and use" the claimed peptides and polypeptides.*

Applicant requests therefore, that the rejection be withdrawn.

The pending claims are not directed to antibody compositions.

The Applicant is perplexed as to why the majority of the present enablement rejection is directed to allegedly deficiencies in enabling antibody compositions, when there are no antibody claims pending. Page 7 of the Action (beginning at the 4th paragraph) states "The scope of the claimed p33-specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claimed invention." The Action continues at the bottom of Page 7 by stating "Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of (*sic*) the claimed p33-specific antibodies in manner (*sic*) reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by the genus of polypeptides as recited in the claims."

This rejection makes no sense, since there are no claims pending to antibodies at all! As Applicant previously noted, the antibody and antigen-binding fragment aspects of the present invention were withdrawn from consideration in the present case after the Office imposed a Restriction Requirement. The pending claims in the present case are directed to isolated peptides and polypeptides, and to compositions and kits which comprise them. That one disclosed use of these peptides is the preparation of antibodies and antigen binding fragments, and that the Examiner considers the Specification is enabling for one of ordinary skill in the art to make and use the disclosed p33-specific antibodies provides clear evidence that Applicant has meet his 112, 1st, burden. The Office concedes that "Applicant has taught how to make and use SEQ ID NOs:2-76

and residues 1-322 of SEQ ID NO:2 to generate antibodies which bind to native p33 to serve as diagnostic markers of therapeutic efficacy of cancer treatments." (the Action at page 8). That alone, is ample evidence that the Specification contains sufficient a written description of the invention.

In fact, the relevant portion of the Statute says:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The Statute does not require the Specification to disclose ***every*** manner and process of making and using the claimed invention, nor does it require that the Specification provide a written description of how to make and use the invention in ***every*** mode, only that it set forth the *best mode contemplated by the inventor* of carrying out his invention. The Specification has done precisely that. It has taught how to make and use the claimed peptides and polypeptides, and has set for the best mode contemplated by the inventor for carrying out the invention (namely, the use of the disclosed epitopic peptides and polypeptides in the generation of immune responses in an animal, and in the creation of antibodies that are specific for the $p33^{QIK}$ and $p63^{KRSI}$ peptides.

A rejection of the present peptide and polypeptide claims allegedly because the Office considers that "theoretical" claims directed to certain species of p33-specific *antibodies* may not be enabled by the Specification is both improper and without merit. The incorrect standard is being applied to examination of the peptide and polypeptide composition claims, and this *prima facie* rejection is improper. Applicant respectfully requests, therefore, that the rejection be withdrawn.

The pending claims are not directed to methods of generating antibodies.

As noted above, the Action admits at page 8 that "Applicant has taught how to make and use SEQ ID NOs:2-76 and residues 1-322 of SEQ ID NO:2 to generate antibodies which bind to native p33 to serve as diagnostic markers of therapeutic efficacy of cancer treatments." However, the Applicant is perplexed why the present enablement rejection is also directed to allegedly deficiencies in the use of these enabled antibody compositions, when there are no antibody claims pending. Page 7 of the Action (beginning at the 4th paragraph) states "The scope of the claimed p33-specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claimed invention." The Action continues at the bottom of Page 7 by stating "Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of (*sic*) the claimed p33-specific antibodies in manner (*sic*) reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by the genus of polypeptides as recited in the claims."

Applicant again reminds the Examiner that all that is required to comply with § 112, 1st paragraph is for the Specification to teach how to make and use the claimed invention so that it may be practiced without undue experimentation (*In re Borkowski and Van Venrooy*, 164 USPQ 642 [C.C.P.A. 1970]). Clearly, the Specification meets this requirement, as it illustrates the materials, methods, and even experimental protocols that may be used to achieve the claimed invention. The requirements for "how to make" and "how to use" have obviously been satisfied in the instant application.

The Examiner has arbitrarily concluded (without providing any affidavit to support the position) that the amount of experimentation "left to those skilled in the art" to understand the claimed invention is "undue." This is improper.

The "need" for experimentation does not render a claimed invention unpatentable under 35 U. S. C. § 112, 1st paragraph. The M. P. E. P. and established case law provide ample support that even if the experimentation is complex, this does not necessarily make it undue, if the art typically engages in such experimentation. (M.P.E.P. §2164.01 citing *M.I.T. v. A.B. Fortia*, 227 USPQ 428). The guidance from the courts is further embodied in the M.P.E.P. at §2164.04, where it is stated that if this [examination] procedure is not followed, there would be no need for the Applicant to go to the trouble and expense of supporting his presumptively accurate disclosure. Indeed, the Courts have held that in fact a *considerable* amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ 2d 1016 (Fed. Cir. 1991).

It is clear from the abundance of U. S. patents cited *supra,* that the objective teachings of the present Specification clearly satisfies the "make and use" requirement of the statute, by providing specific examples of a variety of peptides and polypeptides that comprise, consist essentially of, or consist of one or more amino acid sequences disclosed in the Specification. Whether or not some experimentation would be required to determine which species within the claimed genus would in fact be "antigenic" and thus epitopes able to illicit an immune response in a mammal does not render the genus, itself as lacking enablement or written description. Likewise, the fact that one or more species of the disclosed genus may not function in every known or potential possible use of the peptides (including their use as antigens to illicit an immune response, and as diagnostic markers of the therapeutic efficacy of cancer treatments) does not render the genus non-enabled, either.

Applicant also reminds the Examiner that the Specification need only provide an objective enablement of the claimed invention as required by § 112, 1st paragraph, and that it has been well established that the Specification must be considered as being in compliance with the enabling

requirement of the 1st paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. *In re Marzocchi and Horton*, 169 USPQ 367 (CCPA 1971). The Office has provided no specific, credible reasons to doubt the objective truth of the Specification, and as such, Applicant submits that the present rejection has been overcome and respectfully requests withdrawal of the rejection.

2.5 THE REJECTION OF CLAIMS 1-8, 32-37, 42-52, 61-65, AND 67-75 UNDER 35 U. S. C. §112, 1ST PARAGRAPH, HAS BEEN OVERCOME.

(Re: the Action, Item 9)

The claims have been rejected under 35 U. S. C. §112, 1st paragraph, allegedly for containing subject matter that was not described in the specification in such as way as to reasonably convey to one of skill in the art that the inventor at the time the application was filed, had possession of the claimed invention.

Specifically, the First Action at page 12 stated that:

> "Applicant is in possession of a polypeptide comprising SEQ ID NO:2, a peptide consisting of residues 1-322 of SEQ ID NO:2, and peptides consisting of SEQ ID NOs:3-76, said SEQ ID NO:2/peptides *(sic)* in a pharmaceutically acceptable excipient to be used to generate antibodies which recognize non-human p33 to diagnose the therapeutic effectiveness of cancer treatments; and wherein the immune complexes (said peptides/polypeptide—antibody) can be detected indirectly with another labeled antibody; a kit comprising said peptides" *(sic)*.

The present Action at page 9 states that the rejection is maintained "essentially for the reasons of record set forth" in the first Office Action. Although the present Action states that Applicant's arguments filed 9/25/00 "have been fully considered, but have not been found convincing," the present Action provides absolutely no guidance or analysis of the perceived errors in Applicant's arguments provided in the previous response.

Again, Applicant respectfully traverses.

The Action on page 9 states: "Conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred..." The Action continues, "A description of a genus of polypeptide/peptide sequences may be achieved by means of a recitation of a representative number of polypeptides/peptides having SEQ ID NO:s3-76, residues 1-322 of SEQ ID NO:2, or at least a first peptide and at least a second peptide of SEQ ID NOs:3-76, falling within the scope of the genus, or of a recitation of structural; features common to the genus, which features constitute a substantial portion of the genus." (Citing the decision in Regents of the University of California *v.* Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 [Fed. Cir. 1997]).

Applicant asserts that the present Specification and the pending claims comply fully with that requirement.

Consider claim 1:

First, the genus of peptides encompassed by the claim is described by a recitation of structural features common to the genus:

1) The isolated peptides "are from 14 to about 70 amino acids in length." This is a precise and definite structural feature of the claimed genus. A skilled artisan clearly understands that the genus of peptides does not include peptides smaller than those of 14 amino acids in length, and does not include peptides that are larger than those of about 70 amino acids in length. Isolated peptides of 20, 32, 57, 62, or even 69 amino acids clearly are encompassed by this recitation. This is well-understood by a person of ordinary skill in this art.

2) Moreover, the claimed isolated peptides must "comprise the amino acid sequence of any one of SEQ ID NO:3 through 76." Again, a skilled artisan, referring to the text of the Specification and the appended sequence listing would clearly understand the primary amino acid sequences disclosed in those sequence identifiers that must be comprised with the appropriately-sized peptide

in order to be considered part of the genus of claimed peptides. Simply stated, if a peptide does not comprise at least one of the precise amino acid sequences disclosed in SEQ ID NO:3 through SEQ ID NO:76, then it is not a part of the claimed genus.

Pages 70, 71, and 72 of the Specification provide the clear, concise, and literal primary amino acid sequences of SEQ ID NO:3 through SEQ ID NO:76. One of skill in the art could examine a putative peptide and clearly deduce from those sequences and from the entire Specification whether or not it is a member of the claimed genus, and whether or not the size and the sequence recitation limitations of claim 1 is met.

Moreover, Applicant cannot understand how the Office was not persuaded that the Specification clearly defines the claimed invention. It is clear from the present Action, that the Examiner did not even consider the Applicant's previous response, which directed the Examiner's attention to the Specification at pages 3 bridging page 4 (which clearly and succinctly indicates that one aspect of the invention involves compositions "that comprises at least a first isolated peptide of from 9 to about 80 amino acids in length, or at least a first nucleic acid segment that encodes such a peptide, wherein the peptide comprises, consists essentially of, or consists of a first contiguous amino acid sequence according to any one of SEQ ID NO:3 through SEQ ID NO:76"), or the Specification at pages 5 to 17 (which provides an exhaustive and detailed teaching that extensively describes particular aspects of the invention including how to make and use various polypeptides, peptides, antibodies, antigen binding fragments, epitopic peptides, and the like in a variety of diagnostic and therapeutic regiments), or even more importantly, pages 9 to 20 of the Specification (where a ***lengthy*** teaching is made not only as to the preferred sizes of the disclosed peptides and polypeptides, but also to their preferred primary sequences, as evidenced by a 27-page sequence listing that specifies particularly preferred peptides).

Moreover, the previous response directed the Office's attention to the Specification at pages 21-24, which exhaustively details the use of the novel peptides, polypeptides, antibodies, and antigen binding fragments of the invention (as well as nucleic acid compositions that encode them) in a variety of diagnostic regimens including ELISA, immunoprecipitation, dot blotting, and such like." Similarly, pages 36-40 of the Specification detail the use of these peptide compositions in a variety of diagnostic and therapeutic methodologies, including the production of large quantities of antibodies and antigen binding fragments specific for the disclosed peptides and polypeptide. Moreover, pages 40-44 of the Specification detail the use of nucleic acid compositions that encode these illustrative peptides and polypeptides in a variety of recombinant methodologies, including production of large quantities of these peptides using host cells transformed with such constructs, and pages 51-53 of the Specification were cited in the previous response as evidence of the Specification's detailed description of the use of the disclosed peptide, polypeptide, antibody, antigen binding fragment, and nucleic acid compositions that encode them in a variety of diagnostic and therapeutic kits, including for example immunological detection kits and assays.

In view of the lengthy and detailed teaching of the Specification, Applicant again asserts that both the enablement and written description requirements for how to make and use the disclosed peptides and polypeptides as encompassed by the pending claims are *clearly* and *unambiguously* free from any rejection under this section of the Statute, and respectfully requests that the outstanding rejection be withdrawn.

In conclusion, the Specification provides a description of the genera of claimed polypeptide/peptide sequences not only through the recitation of a representative number of polypeptides/peptides within each genus, but also by the recitation of structural features common to each of the genera.

2.6 THE FAILURE TO GRANT PRIORITY TO THE PROVISIONAL APPLICATION IS IMPROPER.

(Re: the Action, Item 10)

The present Action maintains the previous Action's position that "the filing date of the instant claims is deemed to be that of the instant application, 3/20/2001."

Applicant's arguments have been said to have been fully considered, but have not been found convincing. Once again, this language is lifted verbatim from the previous Action, but no explanation is given as to why the Office is not "convinced" that the present application is entitled to its priority claim.

Again, Applicant is perplexed by the position that the Office has taken with respect to a priority claim, and necessarily traverses. The Action states on page 10 that "Applicant does not clearly pointed out (*sic*) where in provisional application 60/193,550 there are supports (*sic*) for claimed: a) a peptide comprising at least a first contiguous amino acid sequence, pharmaceutically acceptable excipient, immunostimulant, adjuvant, or detection reagent (*sic*)....."

Again, it is respectfully submitted that the written description requirement is not so stringent as to require an exact one-to-one literal correspondence ("at least a first" or "a polypeptide comprising, consisting essentially of, or consisting of") between the language of an original provisional patent specification and claims later advanced in a non-provisional application that claims priority to the earlier document:

> "The function of the description requirement is to ensure that the inventor had possession (as of the filing date of the application relied on) of the specific subject matter latter claimed by him; how the specification accomplishes this is not material. It is not necessary that the application describe the claim limitations exactly, but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that the appellants invented processes including those limitations." *In re Wertheim*, 191 USPQ 90 (C.C.P.A. 1976); emphasis added.

The priority application clearly describes and enables $p33^{QIK}$ or $p63^{Krs1}$ polypeptides and peptides and epitopes derived therefrom, as well as antibodies and antigen binding fragments specific therefor. In contrast to the Action's assertion, the provisional application provides not only an overall description for the claimed invention, but also provides a sequence listing that provided literal written description for the sequences presently identified as SEQ ID NO:3-SEQ ID NO:76.

Denying priority to the provisional application solely on the basis of the fact that the earlier document allegedly provides literal written description for compositions that "comprise" but does not literally disclose compositions that "consist of" or "consist essentially of" a particular claim element is without foundation, and cannot be permitted to stand.

Applicant again notes for the record that case law has already specifically addressed this issue—in *Ruschig* the CCPA found that it was unnecessary for the claimed subject matter to be described in *ipis verbis* to satisfy the written description requirement of § 112. *In re Ruschig*, 154 USPQ 118 (C.C.P.A. 1967); *In re Lukach*, 169 USPQ 795 (C.C.P.A. 1971).

In summary, Applicant again asserts the position that all claims are supported by not only the disclosure of the pending application, but also by the priority non-provisional application, and further believes that all claims are entitled to the effective filing date of the priority application, *i.e.*, March 31, 2000. Applicant respectfully requests that the entitlement of priority be granted.

2.7 THE OBJECTION TO CLAIMS 32 TO 52 IS OVERCOME.

(Re: the Action, Items 11 and 12)

The Action at page 11, objected to claims 32-52 as being objected to for being dependent upon a canceled base claim (claim 11). Applicant has overcome this rejection by remediation of the required claim language to properly depend from pending claim 12.

In light of the foregoing, Applicant respectfully requests that the objection be withdrawn.

2.8 REQUEST FOR RECONSIDERATION OF THE FINALITY OF THE SECOND ACTION

Applicant's undersigned representative contacted Examiner Jamroz in the Office on July 23, 2002 to request an Interview to discuss the issues remaining in the case following the issuance of a first office action, and submission of Applicant's response thereto on July 8, 2002. Applicant's representative was denied that request; however, as Examiner Jamroz indicated that the case would likely be reassigned to a new Examiner for reasons not explained to the representative. Examiner Jamroz indicated, however, that when the case was transferred, she would discuss Applicant's request with the new Examiner, and that the Office would contact Applicant's representative to schedule the interview as previously requested in the response dated July 8, 2002.

Applicant's representative was not contacted by the Office, and in August, 2002 discovered that Examiner Jamroz was no longer assigned to the art unit. Likewise, on October 9, 2002, Applicant then received a final office action from the new examiner, Examiner Michail Belyavskyi. Following consultant with the assignee of record, Applicant's representative contacted Examiner Belyavskyi on January 9, 2003 to arrange an Interview to discuss the case during Applicant's representative's upcoming visit to the Patent Office. Examiner Belyavskyi advised, however, that he would be unable to interview the case without the presence of Supervisory Examiner Christina Chan, and that Examiner Chan would be unavailable for an Examiner Interview during the period of

January 15-17, 2003 when Applicant's undersigned representative was scheduled at the Office to conduct interviews with various other Examiners in Technology Center 1600.

Therefore, owing to a change of examiners, and neither examiner's availability to conduct an interview on the record at a time convenient to Applicant's representative prior to the issuance of a final office action, pursuant to M. P. E. P. §706.07(d), Applicant respectfully requests that the Primary Examiner reconsider the finality of the present Action, and to withdraw the finality as being premature, particularly to facilitate entry of the present amendment, and consideration of the merits of the present response. As Applicant is a small-entity inventor, and the expense of filing a Brief on Appeal, or a Request for Continued Examination would be a substantial economic hardship, Applicant requests that the finality of the present Action be withdrawn so that the present amendment be entered and the remarks thereon properly considered by the new Examiner, and his supervisor, Examiner Chan.

2.9 REQUEST FOR RECONSIDERATION OF FINALITY OF SECOND ACTION

In the alternative, should the Primary Examiner decline to remove the finality of this second action even in view of the above circumstances, and moreover in view of the fact that:

(1) certain claims have already been allowed; (2) no issues of prior art remain; and (3) Applicant has diligently endeavored to address the remaining rejections, even with a change of Examiners mid-case, and without the benefit of an official Interview on the record from either primary examiner, pursuant to 37 C. F. R. § 1.116(b), Applicant hereby requests that the present amendment be entered and the remarks considered therein, as they clearly touch on the merits of the application, and clearly place the claims in condition for allowance. This is consistent with the intent of 37 C. F. R. § 1.116(b), which states in pertinent part "(i)f amendments touching the merits

of the application...are presented after final rejection....they may be admitted upon a showing of good and sufficient reasons why they are necessary and were not earlier presented."

2.10 THIRD REQUEST FOR EXAMINER INTERVIEW

Owing to a change in the Examiner-in-Charge of the present application, and Applicant's inability to schedule an interview on the record to discuss progression of the claims to allowance, pursuant to M. P. E. P. § 713.01 and 37 C. F. R. §1.133, Applicant again hereby formally requests the scheduling of an Interview with the Examiner-in-Charge, the Examiner's Supervisory Patent Examiner, and Applicant's undersigned representative to discuss the claims as are now in condition for allowance, and to address any particular remaining issues in the mind of the Examiner once he has had the opportunity to review this response.

Further pursuant to M. P. E. P. § 713.09, Applicant notes that the grant of such an interview is deemed proper *even if the finality of the present rejections are maintained.*

2.11 SUMMARY

In conclusion, in light of the foregoing remarks, Applicant believes that the concerns set forth in the Action have now been overcome and that all pending claims are in condition for immediate allowance. Such favorable action is respectfully requested. Should the Examiner have any questions concerning the accompanying amendment, response and related papers, a telephone call to Applicant's undersigned representative would be greatly appreciated.

Respectfully submitted,

Date: March 31, 2003

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AGENT FOR APPLICANT

EXHIBIT A

MARKED-UP CLAIMS SHOWING AMENDMENTS FOR U.S. SERIAL NO. 09/822,110, WANG

1. (Twice Amended) An isolated peptide of from [9]14 to about 70 amino acids in length, said peptide comprising the amino acid sequence of any one of SEQ ID NO:3 through SEQ ID NO:76.

2. (Amended) The isolated peptide of claim 1[, of from 9 to about 60 amino acids in length]said peptide consisting essentially of the amino acid sequence of any one of SEQ ID NO3 through SEQ ID NO:76.

3. (Amended) [The]An isolated peptide [of claim 2,]of from [9]14 to about 50 amino acids in length, said peptide comprising the amino acid sequence of any one of SEQ ID NO:3 through SEQ ID NO:55 or any one of SEQ ID NO:58 through SEQ ID NO:76.

4. (Amended) [The]An isolated peptide [of claim 3,]of from [9]14 to about 40 amino acids in length, said peptide comprising the amino acid sequence of any one of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:15 through SEQ ID NO:52, SEQ ID NO:58 through SEQ ID NO:67, or SEQ ID NO:74 through SEQ ID NO:76.

5. (Amended) [The]An isolated peptide [of claim 4,]of from [9]14 to about 30 amino acids in length, said peptide comprising the amino acid sequence of any one of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:25 through SEQ ID NO:50, or SEQ ID NO:74 through SEQ ID NO:76.

6. (Amended) [The]An isolated peptide [of claim 5,]of from [9]14 to about 20 amino acids in length, said peptide comprising the amino acid sequence of any one of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:46 through SEQ ID NO:50.

8. (Twice Amended) [The]An isolated peptide [of claim 1, said peptide]consisting essentially of the amino acid sequence of any one of SEQ ID NO:3 through SEQ ID NO:76.

9. (Twice Amended) [The]An isolated peptide [of claim 8, said peptide]consisting of the amino acid sequence of any one of SEQ ID NO:3 through SEQ ID NO:[76]36.

32. (Thrice Amended) The isolated peptide of claim 1, or the polypeptide of claim [11]12, further comprising at least [a first]one detectable label.

33. (Thrice Amended) The isolated peptide or polypeptide of claim 32, wherein said at least one[a first]detectable label is a radiolabel, a chromogenic label, a fluorescent label or a labelled secondary antibody that specifically binds to said peptide or said polypeptide.

37. (Amended) The isolated peptide or polypeptide of claim 36, wherein said fluorescent protein comprises at least one [a first]green fluorescent protein or at least [a first]one humanized green fluorescent protein.

42. (Thrice Amended) A composition comprising: the isolated peptide of claim 1, or the polypeptide of claim [11]12.

43. (Amended) The composition of claim 42, further comprising at least [a first]one pharmaceutically-acceptable excipient.

44. (Amended) The composition of claim 42, further comprising at least [a first]one immunostimulant or at least [a first]one adjuvant.

45. (Amended) The composition of claim 44, wherein said at least [a first]one immunostimulant or said at least [a first]one adjuvant is selected from the group consisting of a cytokine, a microsphere, Ribi Adjuvant, saponin, a microfluidized adjuvant, an immune stimulating complex, and an inactivated toxin.

47. (Amended) The composition of claim 42, further comprising at least [a first]one detection reagent.

49. (Amended) The composition of claim 48, wherein said at least [a first]one detection reagent specifically binds to (a) a $p33^{QIK}$ peptide or polypeptide; (b) a $p63^{Krs1}$ peptide or polypeptide, (c) an antibody or an antigen binding fragment specific for a $p33^{QIK}$ peptide or polypeptide, or (d) an antibody or an antigen binding fragment specific for a $p63^{Krs1}$ peptide or polypeptide.

50. (Amended) A kit comprising the isolated peptide of claim 1, the isolated polypeptide of claim [11]12, or an antibody or an antigen binding fragment specific for either the isolated peptide of claim 1 or the isolated polypeptide of claim [11]12; and instructions for using said kit.

61. (Amended) The isolated peptide of claim [7]66, said peptide [comprising]consisting of the amino acid sequence of SEQ ID NO:3.

62. (Amended) The isolated peptide of claim [7]66, said peptide [comprising]consisting of the amino acid sequence of SEQ ID NO:4.

63. (Amended) The isolated peptide of claim [7]66, said peptide [comprising]consisting of the amino acid sequence of [SEQ ID NO:5]any one of SEQ ID NO:5 through SEQ ID NO:36.

67. (Amended) An isolated peptide of from 14 to [about]approximately 50 amino acids in length, said peptide comprising the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5.

68. (Amended) The isolated peptide of claim 67, wherein said peptide is from 14 to [about]approximately 45 amino acids in length.

69. (Amended) The isolated peptide of claim 67, wherein said peptide is from 14 to [about]approximately 40 amino acids in length.

70. (Amended) The isolated peptide of claim 67, wherein said peptide is from 14 to [about]approximately 35 amino acids in length.

71. (Amended) The isolated peptide of claim 67, wherein said peptide is from 14 to [about]approximately 30 amino acids in length.

72. (Amended) The isolated peptide of claim 67, wherein said peptide is from 14 to [about]approximately 25 amino acids in length.

73. (Amended) An isolated peptide of from 14 to [about]approximately 70 amino acids in length, said peptide comprising [an]the amino acid sequence [selected from]of any one of SEQ ID NO:3 through SEQ ID NO:76.

74. (Amended) An isolated peptide of from 14 to [about]approximately 60 amino acids in length, said peptide comprising [an]the amino acid sequence [selected from]of any one of SEQ ID NO:3 through SEQ ID NO:76.

75. (Amended) An isolated peptide of from 14 to [about]approximately 50 amino acids in length, said peptide comprising [an]the amino acid sequence [selected from]of any one of SEQ ID NO:3 through SEQ ID NO:76.